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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/615,703	BENKOVIC ET AL.	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,12-14 and 45-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,12-14 and 45-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims Status

Claims 1-2, 12-14 and 45-50 are pending and under consideration.

Withdrawn Rejections

In view of the amendments to the claims the following rejections have been withdrawn: 35 USC 101, 35 USC 112, second paragraph; double patenting and the 35 USC 103 over Vermeulen et al in view of Barney et al and Lonetto et al.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1-2, 12-14 and 45-50, as amended, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons as set forth in the last Office action as reiterated below.

The specification does not provide an adequate written description of a methyltransferase inhibitor of the claimed genus that has been administered to a mammal to therapeutically treat mammals afflicted with a bacterium induced disease such as Brucella species. The original specification describes a method of inhibiting specific disease causing DNA methyltransferase utilizing specific compounds e.g., 1-5 at page 92 having a defined structures thereof, not in a pharmaceutical composition. There is no description of a genus corresponding to the species that is employed in the method. It is not apparent from the description whether the experimental conditions employed for the species is applicable to the genus of such huge scope. The genus covers every conceivable combinations of the given moieties attached to the different compounds. A lack of adequate written description issue arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559,1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead"

those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967).

Response to Arguments

Applicants state that biological data that demonstrates inhibition of bacterial cell growth via inhibition of DNA methyltransferase is disclosed in the specification. See, for example, pages 35, 92-94, and 122-124.

In reply, a review of the above cited sections describe specific compounds not the claimed genus.

New Matter Rejection

The claimed method which recites administering a composition comprising of the compound of the given structure to treat a human is not supported in the as-filed specification. The as-filed specification recites said compound(s) with a given structure to obtain specific compound(s) which is then used to treat a bacterium. Furthermore, the claimed proviso "if A is O, X is not present, and Ar1 and Ar2 are not conjoined, then p is not 0" is also not supported in the original disclosure. MPEP 714.02 clearly states that applicants point out where in the specification support can be found for the new claimed limitations.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 12-14 and 45-50,, as amended, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 1 is confusing in that the preamble recites treating a **human** which is at odds with the body of the claim which recites an **animal** in need of such treatment.

2. Claim 1 is unclear as the metes and bound of the claimed substituted embodiments are not clearly set forth in the specification. The specification does not define or define what constitutes an embodiment(s). This rejection has similar import to claims 45-47 and 51. Furthermore, it is not clear whether e.g., Ar1 and Ar2 substituents are all different at the different positions of the aryl ring.

3. Claim 12 is indefinite since the base claim 1 from which it depends is drawn to a method not to a compound (product) DNA methyl transferase inhibitor.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2, 12-14 and 45-50, as amended, are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims e.g., 20-42 of copending Application No. 2005005464('644 published application) or over claims 19-23 of 20040259833 ('833 published application).

The '644 or '833 application discloses the same method of treating bacteria e.g., Helicobacter as the instant method utilizing the same boron containing compounds. The claimed inhibition of DNA methyltransferase is a property inherent to the compound used in the method, (see the '644 published application).

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claims 1-2, 12-14 and 45-50, as amended of this application conflict with claims 20-42 of copending Application No. 2005005464('644 published application) or over claims 19-23 of 20040259833 ('833 published application). 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either

cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2, 12-14 and 45-50, as amended, are rejected under 35 U.S.C. 102(e) as being anticipated by Lee et al (2005005464) or Benkovic et al (20040259833). The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this

application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

See the rejection above under 35 USC 101 double patenting rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 12-14 and 45-50, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable Patel et al (5348947) in view of Vermeulen et al (5872104) and Barney et al (6068973)and Lonetto et al (6165762).

Patel discloses throughout the patent at e.g., the claims a method of treating fungus by administering a diarylboron ester and thioester having the formula as shown at e.g., the abstract. Patel does not disclose that said diarylboron ester can treat a DNA methyltransferase mediated bacteria induced disease.

Vermeulen discloses throughout the patent at e.g., col. 3, lines 4-64:

> A method comprising administering to an animal (including a human patient) that has, or is suspected to have a microbial or bacterial infection, a therapeutically effective amount of pharmacologically acceptable antimicrobial agent formulation in combination with a therapeutic amount of a pharmacologically acceptable formulation of a second agent effective to inhibit methylation, e.g., effective to inhibit RNA methylation. The invention may thus be employed to treat both systemic and localized **microbial** and bacterial infections by introducing the combination of agents into the general circulation or by applying the combination, e.g., topically to a specific site, such as a wound or burn, or to the eye, ear or other site of infection.
>
> The "second agents" for use in the invention are generally methylation inhibitors, and are also referred to herein as "inhibitors" and "modifiers". The second agent inhibitors should be used in amounts effective to inhibit methylation in a microorganism or bacterium, as exemplified by an amount effective to inhibit RNA methylation, synthesis and/or maturation in an MLS-susceptible bacterium. Suitable amounts effective to inhibit methylation will be known, or readily identifiable, to those of skill in the art. Effective inhibitory amounts are the amounts that have previously been shown in the scientific literature to inhibit methylation generally or to inhibit a specific methylation step. In addition to the present disclosure and the references specifically incorporated herein, there is considerable scientific literature concerning methylation inhibitors that may be utilized in light of the inventors' discovery that such compounds may be effectively combined with antibiotics and other antimicrobial agents.
>
> Amounts effective to inhibit methylation may also be measured, rather than identified from the published literature. Most simply, this is achieved by determining the amount effective to increase microbial or bacterial killing when used in combination with an antimicrobial

> agent, i.e., by determining an amount effective to reduce antimicrobial resistance. The determinations of effective inhibitory amounts and therapeutic doses will be routine to those of skill in the art given the teachings of the present disclosure, including the detailed methodology and the effective amounts of various agents disclosed, e.g., in Table 8 and throughout the detailed examples.

Patel does not disclose bacteria. However, Vermeulen discloses in general bacteria and microbes.

Barney et al throughout the patent discloses the different bacterial species such as Agrobacterium, Rhizobium and Helicobacter. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to treat bacteria or other microbes such as fungi in the method of Patel in view of Vermuelen's disclosure that not only bacteria are treated by inhibitors of DNA methylase but other microbes as well. One having ordinary skill in the art would know that a fungus is one type of microorganism(s) as taught by Vermuelen. Vermeulen teaches treatment of bacteria in general and does not seem to limit to those disclosed therein. It would be within the ordinary skill in the art at the time the invention was made to choose the specific bacteria depending upon the bacteria desired to be treated. The bacteria Agrobacterium, Rhizobium and Helicobacter are known to have been treated in the art whether via the

mechanism of DNA methyltransferase inhibition or by other mechanistic pathway as evidenced by Lonetto et al, which discloses at e.g., col. 19, lines 50-67:

> Helicobacter pylori (herein H. pylori) bacteria infect the stomachs of over one-third of the world's population causing stomach cancer, ulcers, and gastritis (International Agency for Research on Cancer (1994) Schistosomes, Liver Flukes and Helicobacter Pylori…….. Moreover, the international Agency for Research on Cancer recently recognized a cause-and-effect relationship between H. pylori and gastric adenocarcinoma, classifying the bacterium as a Group I (definite) carcinogen. Preferred antimicrobial compounds of the invention (agonists and antagonists of apt) found using screens provided by the invention, particularly broad- spectrum antibiotics, should be useful in the treatment of H. pylori infection. Such treatment should decrease the advent of H. pylori-induced cancers, such as gastrointestinal carcinoma.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TERESA WESSENDORF/

Primary Examiner, Art Unit 1639

July 31, 2008